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Energy Restriction in Childhood and Adolescence and Risk of Prostate Cancer: Results from the Netherlands Cohort Study

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This study investigated the association between prostate cancer risk and energy restriction during childhood. The authors examined the hypothesis among 58,279 men aged 55–69 years enrolled in the Netherlands Cohort Study on Diet and Cancer. Information on diet and risk factors was collected by questionnaire in 1986. Additional information was collected on residence during the Dutch Hunger Winter (1944–1945) and the World War II years (1940–1944) and father's employment status during the economic depression of 1932–1940, used as indicators of exposure. A case-cohort approach was used. After 7.3 years of follow-up (through December 1993), 903 prostate cancer cases were available for analysis. Analyses were carried out for all prostate cancer cases. The prostate cancer rate ratio for men who had lived in a western Netherlands city in 1944–1945 was 1.15 (95% confidence interval (CI): 0.80, 1.31), and the rate ratio for men who had lived in a western rural area in 1944–1945 was 1.30 (95% CI: 0.97, 1.73). Residence during the war years (1940–1944) and father's employment in 1932–1940 showed no relation to prostate cancer risk. In subgroup analyses in which exposure before, during, and after the adolescent growth spurt was evaluated, the same pattern as that of the overall data was shown. The authors found no evidence for the hypothesis that energy restriction early in life decreases prostate cancer risk later in life. *Am J Epidemiol* 2001;154:530–7.

diet; energy intake; food deprivation; prostatic neoplasms

Prostate cancer is the second most commonly diagnosed cancer in males after lung cancer. The age-standardized incidence rate in the Netherlands in 1994 was 87.2 per 100,000 males (1). In addition, the number of newly diagnosed patients with prostate cancer has recently increased considerably (1).

The role of dietary risk factors in the development of prostate cancer is not clear. Ross and Henderson (2) stated that diet can alter steroid hormone profiles and thereby modify prostate cancer risk throughout life. Their model suggests that diet-regulated hormonal influences first exert an effect in utero. Ross and Henderson speculated that high testosterone levels during pregnancy may contribute to high rates of prostate cancer in male offspring. A high-fat diet during childhood could also contribute to early puberty and to prolonged exposure to testosterone. It has been hypothesized that exposure to a high-fat diet during adolescence may initiate tumor development. Diamandis and Yu (3) speculated that in early life, especially around puberty, when there is an abrupt and massive increase of steroid hormone production by the testes, prostate cells may undergo malignant transformation and start to proliferate (4, 5).

Several studies have evaluated the relation between diet and prostate cancer, but only a few have concentrated on diet in adolescence. Slattery et al. (6) conducted a case-control study of prostate cancer in which reported food consumption patterns for the adolescent and adult years were assessed. Men who had had a diet high in saturated fatty acids as adolescents were not at increased risk of developing prostate cancer. Another study (7) evaluated the relation of dietary and lifestyle characteristics to subsequent prostatic cancer risk in a cohort of 14,000 Seventh-day Adventist men. In that study, exposure to a vegetarian diet during childhood was not associated with prostate cancer risk later in life. Results of a case-control study carried out in Sweden (8) showed no clear association between dietary habits during childhood and adolescence and prostate cancer risk. To investigate the relation between early dietary exposures and later cancer risk, proxy measures are generally needed, because no individual data on diet early in life are available.

In the Netherlands, a substantial portion of the population experienced severe famine in World War II, during the so-called Hunger Winter of 1944–1945. The famine especially affected the western part of the country. This unique setting has provided researchers with an opportunity to study the effects of severe undernutrition during adolescence on risk of prostate cancer later in life (9–11). In addition, a period

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Abbreviations: CI, confidence interval; PALGA, Pathologisch Anatomisch Landelijke Geautomatiseerd Archief; RR, rate ratio.

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of chronically impaired nutrition existed in the Netherlands during the earlier years of World War II (1940–1944) and the economic depression of the 1930s. As a consequence of the poor availability of food products in the cities, nutritional differences developed between residents of cities and residents of rural areas during the war years (12, 13). During the economic depression, a large proportion of people were unemployed. Several surveys showed that there was little variation in the food patterns of families with an unemployed breadwinner and that their energy intake was not at the same level as that of the families of employed people (14–17). The energy restriction during these three periods—the economic depression, the war years, and the Hunger Winter—was the subject of investigation in this study.

We examined the association between diet in childhood and adolescence and prostate cancer risk in the Netherlands Cohort Study on Diet and Cancer. Men who had been in their pubertal years during the economic depression, World War II, and the Hunger Winter were included in this prospective cohort study. We also examined interactions with the age at which dietary restriction had taken place.

MATERIALS AND METHODS

The Netherlands Cohort Study started in September 1986 when 58,279 men aged 55–69 years were enrolled in the cohort. The total cohort comprises the 120,852 subjects who completed the baseline questionnaire, which was sent to 340,439 persons (response rate = 35.5 percent). The subjects originated from 204 municipal population registries throughout the country. Baseline exposure data were collected by means of a self-administered questionnaire. The questionnaire referred to dietary habits and potentially confounding factors such as physical activity, anthropometric measurements, smoking, education, and family history of cancer. Also included were questions about the residences of cohort members, including residence in the winter of 1944–1945, and father's employment status during the economic depression. A detailed description of the cohort study's design has been reported elsewhere (18). After the baseline exposure measurement, a subcohort was randomly sampled from the cohort and was followed biennially by questionnaire for information on vital status, drug use, and occurrence of other diseases. Incident cancer cases occurring in the entire cohort were identified through record linkage to cancer registries and a national pathology register (Pathologisch Anatomisch Landelijke Geautomatiseerd Archief (PALGA)). The method of record linkage has been described previously (19).

In order to minimize potential observer bias in coding and data interpretation, data from the subcohort and from prostate cancer cases were key-entered twice by research assistants who were blinded with respect to subcohort/case status. The present analysis was restricted to cancer incidence during the 7.3-year follow-up period from September 1986 to December 1993. Completeness of cancer follow-up exceeded 96 percent (20). After these 7.3 years of follow-up, 903 prostate cancer cases were available for analysis, after exclusion of prevalent cases. Prevalent cases of cancers other than skin cancer were also excluded from the subcohort, after which 1,630 men remained for analysis. Data analysis used the case-cohort approach, in which cases are derived from the entire cohort while person-years at risk are estimated from the subcohort.

Assessment of energy restriction

The exposure variables had to adequately represent the energy restriction experienced by the men in the cohort during the economic depression (1932–1940), the war years (1940–1944), and the Hunger Winter (1944–1945). Data on the men's intake of individual foods during these periods were not available; therefore, we used proxy variables for the energy restriction incurred during each of these periods. For the economic depression years (1932–1940), the occupation of the subject's father was the best available proxy variable. Having an unemployed father during those years was taken to indicate that the amount of calories available had been sufficient but the variation in the subject's food pattern had been limited. The exposure variable for the economic depression years was dichotomous: men whose father had had a job during most of the period and men whose father had had no job during that period. For the World War II period (1940–1944) and the Hunger Winter (1944–1945), city of residence during the period was taken to approximate exposure to energy restriction. Living in a city with more than 40,000 inhabitants in 1942 (the midpoint year of 1940–1944) was considered an indicator for energy restriction during the war, because of the documented nutritional differences between cities and rural areas (13). This exposure variable was dichotomous (living in a city in 1942 vs. living in a rural area in 1942). With respect to the Hunger Winter, three categories were defined: men who had lived in a western city, men who had lived in a western rural area, and men who had lived in a nonwestern part of the Netherlands. Living in a western city in 1944–1945 was considered an indicator for severe energy restriction. The definition of a famine city (>40,000 inhabitants) was based on the definition used in the study by Stein et al. (21).

In addition, the timing of exposure was considered. During the adolescent growth spurt of boys, energy restriction may have a considerable impact on later cancer risk. If less energy is available during the growth spurt, cell division may be slowed, making cells less susceptible for initiating carcinogenic factors (2). Adolescent growth spurt, as used in this study, was taken to occur between the ages of 12 and 15 years (22). For men who had been in the adolescent growth spurt, the three exposure periods were defined more specifically. Since the exposure periods were age-dependent and of varying durations, we decided to restrict the relevant time span in the long exposure periods, 1932–1940 and 1940–1944, to the years in which the food situation was worst. For the economic depression period, we selected the years 1933–1934, because the literature on the economic depression showed a very poor food situation in the early years and some improvement in the later years. Thus, only men with an adolescent growth spurt in 1933–1934 were included in that subgroup. The age range was 2–11 years for

men who had been exposed in the depression years before their adolescent growth spurt. For the World War II period, we selected the years 1942–1943, because the food situation deteriorated progressively during the war and the years 1942–1943 represented the worst years of the prefamine period. The men who had been exposed in the war years before their adolescent growth spurt were all 11 years old at the time.

Data analysis

The data distributions of exposure variables for the prostate cancer cases and the male subcohort members were compared. Associations between exposure variables and covariates were also studied in the subcohort. For the continuous covariates age, height, Quetelet index (23), and intakes of energy and β-cryptoxanthin (24) at baseline, mean values were compared between the exposure categories. The statistical significance of these associations was tested by *t* test and analysis of variance. Chi-squared tests were also conducted for associations between exposure categories and categorical covariates. Covariates associated with prostate cancer itself or with any of the exposure variables were considered as potential confounders. Age, family history of prostate cancer, educational level, intakes of β-cryptoxanthin and energy at baseline, marital status, and height were considered as confounders because they were associated with the exposure variables.

All analyses were carried out using GLIM software (25). Data were analyzed using the case-cohort approach, calculating age-adjusted rate ratios for prostate cancer and 95 percent confidence intervals. Tests for trend were based on likelihood ratio tests. In multivariate analyses, adjustment for covariates was carried out. To assess whether the effect of energy restriction on prostate cancer risk was modified by the timing at which dietary restriction took place, prostate cancer rate ratios for energy restriction in each of the three study periods were calculated within strata of the adolescent growth spurt. Rate ratios were also computed in subgroups of localized, advanced, and latent prostate tumors. The classification into localized tumors (T0–2, M0) and advanced tumors (T3–4, M0: T0–4, M1) was based on the tumor-node-metastasis (TNM) staging system (26). On the basis of information from the pathology reports, which we obtained from PALGA, prostate cancer cases detected during transurethral prostate resections were coded as latent. Cases detected during surgical procedures related to suspected cancer (biopsy, radical prostatectomy) were coded as nonlatent (24). Cases were excluded from these subgroup analyses when this additional information was unknown or unclear (38.1 percent).

RESULTS

Table 1 shows the distributions of the exposure variables among prostate cancer cases and the male subcohort. Table 2 presents overall mean values for continuous variables and the distributions of categorical variables in relation to the exposure categories among subcohort men.

For the Hunger Winter period, height, intakes of energy and β-cryptoxanthin, having a brother with prostate cancer, educational level, and marital status differed between the three exposure categories. Men who had lived in a western rural area during the winter of 1944–1945 were taller and had the highest energy intake in 1986 compared with men who had lived in a western city or in some other part of the Netherlands during that winter. Men who had lived in a western city during the Hunger Winter had the highest level of β-cryptoxanthin intake compared with men living in other parts of the Netherlands. For the World War II years (1940–1944), weight, energy intake, β-cryptoxanthin intake, and educational level were significantly different between the exposure categories. Men who had lived in a city during the war years were less heavy than men who had lived in a rural part of the country during the war. Baseline energy intake was significantly lower and intake of β-cryptoxanthin was significantly higher for men living in a city in 1942 as compared with a rural area. Men whose fathers had had no job during the economic depression years were considerably

TABLE 1. Distribution of data on energy-restriction exposure variables in prostate cancer cases and a male subcohort, Netherlands Cohort Study, September 1986–December 1993

Exposure variable	Cases* (*n* = 903)		Subcohort* (*n* = 1,630)	
	No.	%	No.	%
Hunger Winter (1944–1945)				
Residence in a nonwestern area	396	56.3	794	59.8
Residence in a rural western area	126	17.9	199	15.0
Residence in a western city	181	25.8	334	25.2
World War II years (1940–1944)				
Residence in a rural area	306	45.7	576	49.8
Residence in a city with >40,000 inhabitants	346	54.3	581	50.2
Economic depression (1932–1940)				
Father had a job	749	88.6	1,343	87.9
Father had no job	96	11.4	185	12.1

* Because of missing data, numbers in categories may not added up to 930 and 1,630.

TABLE 2. Mean values for continuous variables and percentages for categorical variables, by energy-restriction exposure category, among members of a male subcohort (*n* = 1,630), Netherlands Cohort Study, 1986–1993

Subcohort characteristic	Exposure category†													
	Hunger Winter (1944–1945)						World War II years (1940–1944)				Economic depression (1932–1940)			
	Residence in a nonwestern area (*n* = 794)		Residence in a western rural area (*n* = 199)		Residence in a western city (*n* = 334)		Residence in a rural area in 1942 (*n* = 576)		Residence in a city of >40,000 in 1942 (*n* = 582)		Father had a job (*n* = 1,349)		Father had no job (*n* = 187)	
	Mean or %	SD‡	Mean or %	SD	Mean or %	SD	Mean or %	SD	Mean or %	SD	Mean or %	SD	Mean or %	SD
Mean age (years) in 1986	61.0	4.2	60.7	4.2	61.2	4.4	61.1	4.2	61.6	4.2	61.3	4.2	61.5	4.3
Mean height (cm) in 1986	176.1	6.6	178.9	7.0	177.0***	6.6	176.6	7.0	176.2	6.7	176.8	6.8	176.6	7.4
Mean weight (kg) in 1986	78.5	9.7	78.0	9.7	77.8	9.5	79.0	9.9	77.0**	9.6	78.2	9.7	77.9	9.9
Mean weight at age 20 years	68.3	8.0	68.0	9.2	67.6	8.1	68.4	8.1	67.4	8.6	67.8	8.3	68.0	9.8
Mean Quetelet index§	24.8	2.7	24.4	2.6	25.3	2.7	25.3	2.7	24.8	2.6	25.0	2.6	24.9	2.8
Mean energy intake (kcal/day) in 1986	2,161	543	2,180	517	2,071***	472	2,173	537	2,091**	494	2,152	519	2,083	509
Mean β-cryptoxanthin intake (μg/day) in 1986	134	140	141	150	163***	175	128	143	162**	159	148	159	146	158
Father with prostate cancer (%)														
No	98.0		97.0		98.5		98.3		97.2		97.6		98.4	
Yes	2.0		3.0		1.5		1.7		2.8		2.4		1.6	
Brother with prostate cancer (%)														
No	100.0		99.0		99.4*		99.7		99.7		99.8		99.5	
Yes			1.0		0.6		0.3		0.3		0.2		0.5	
Level of education (%)														
Low	53.2		50.8		37.5*		61.5		43.3*		45.9		64.1*	
Medium	30.9		32.2		38.7		28.3		40.3		36.0		23.4	
High	15.9		17.0		23.8		10.2		16.4		18.1		12.5	
Marital status (%)														
Single	4.4		4.1		4.5*		3.5		4.0		4.3		1.6	
Divorced	3.8		0.5		4.5		2.6		4.8		3.6		4.9	
Married	86.4		93.4		86.7		89.5		86.0		87.6		86.4	
Widowed	5.4		2.0		4.3		4.4		5.2		4.5		7.1	

* $p < 0.05$ (χ^2 test); ** $p < 0.005$ (*t* test); *** $p < 0.001$ (analysis of variance).
† Because of missing values, numbers in categories may not add up to 1,630.
‡ SD, standard deviation.
§ Weight (kg)/height $(m)^2$.

less educated than men whose fathers had had a job during the depression.

Table 3 shows results from the age-adjusted and multivariate analyses of exposure in the three periods and prostate cancer risk. For the Hunger Winter, multivariate analyses showed an increased risk (rate ratio (RR) = 1.30, 95 percent confidence interval (CI): 0.97, 1.73) for men living in a western rural area compared with other parts of the Netherlands. A small elevated risk was also seen for men living in a western city (RR = 1.15, 95 percent CI: 0.80, 1.31) compared with other parts of the Netherlands. For exposure during the remaining war years, a risk of 1.12 (95 percent CI: 0.90, 1.40) was seen for men who had lived in a city in 1942 as compared with a rural area. With respect to the economic depression years, age-adjusted and multivariate analyses showed the same results as the overall results. A small decrease in risk was seen for men whose fathers had been unemployed during the depression years (age-adjusted RR = 0.93, 95 percent CI: 0.70, 1.22; multivariate RR = 0.95, 95 percent CI: 0.71, 1.27).

We conducted several subgroup analyses to evaluate possible effects of the timing of energy restriction (see table 4). As a consequence of our definition of the adolescent growth spurt (ages 12–15 years), the subgroup for exposure before the growth spurt during the Hunger Winter contained no cohort members. All of the men had been older than 12 years at the time of the Hunger Winter.

Exposure to energy restriction during the adolescent growth spurt showed no elevated risk (RR = 1.01, 95 percent CI: 0.46, 2.22) for men who had lived in a western city during the Hunger Winter as compared with nonwestern parts of the Netherlands. For men living in a western rural area during the Hunger Winter, a slightly increased risk (RR = 1.86, 95 percent CI: 0.85, 4.07) was seen in comparison with living in a nonwestern part of the Netherlands during that winter, but the number of cases was very small and the 95 percent confidence interval was accordingly large. During the war years, a slightly increased risk of prostate cancer (RR = 1.17, 95 percent CI: 0.70, 1.95) was seen for men living in a city in 1942 during their adolescent growth spurt in comparison with men who were living in a rural area in 1942. The rate ratio for men whose fathers had had no job in 1933–1934 and who were in their adolescent growth spurt at that time showed a slight decrease in prostate cancer risk (RR = 0.93, 95 percent CI: 0.57, 1.52). The subgroup exposed after the adolescent growth spurt showed a decreased risk (RR = 0.53, 95 percent CI: 0.20, 1.38) for men whose fathers were unemployed during the depression years, but the number of cases was small. For men exposed before their adolescent growth spurt and whose fathers were unemployed during the depression years, a small increased risk was seen (RR = 1.10, 95 percent CI: 0.74, 1.64).

We also conducted multivariate analyses for energy restriction in the three time periods separately for localized, advanced, latent, and nonlatent tumors. In the subgroup with localized prostate tumors, men living in a western city showed a decreased risk (RR = 0.84, 95 percent CI: 0.58, 1.21) compared with men living in other parts of the country. The other subgroup analyses for the other exposure peri-

TABLE 3. Age-adjusted and multivariate rate ratios for prostate cancer according to energy-restriction exposure during three time periods (7.3 years of follow-up), Netherlands Cohort Study, 1986–1993

Exposure variable	Age-adjusted* analysis				Multivariate analysis				
	No. of cases (cohort)	Person-years of observation (subcohort)	Rate ratio	95% confidence interval	No. of cases (cohort)	Person-years of observation (subcohort)	Rate ratio†	95% confidence interval	Rate ratio‡	95% confidence interval
Hunger Winter (1944–1945)										
Residence in a nonwestern area	396	5,449	1.00§		363	4,914	1.00§		1.00§	
Residence in a western rural area	126	1,391	1.34	1.02, 1.75	113	1,260	1.30	0.97, 1.73	1.32	0.99, 1.76
Residence in a western city	181	2,277	1.09	0.87, 1.37	168	2,090	1.15	0.80, 1.31	1.14	0.79, 1.30
World War II years (1940–1944)										
Residence in a rural area in 1942	306	3,969	1.00§		269	3,540	1.00§		1.00§	
Residence in a city of >40,000 in 1942	364	3,975	1.13	0.93, 1.38	342	3,677	1.12	0.90, 1.40	1.12	0.90, 1.40
Economic depression (1932–1940)										
Father had a job	749	9,295	1.00§		681	8,515	1.00§		1.00§	
Father had no job	96	1,265	0.93	0.70, 1.22	87	1,085	0.95	0.71, 1.27	0.97	0.72, 1.31

* Age in three categories: 55–59 years, 60–64 years, and 65–69 years.
† Adjusted for age, prostate cancer in family, energy intake in 1986 (kcal/day), education, marital status, height, and β-cryptoxanthin intake in 1986 (μg/day).
‡ Multivariate model that excluded height.
§ Reference category.

TABLE 4. Rate ratios for prostate cancer among men exposed to energy restriction before, during, or after their adolescent growth spurt (defined as ages 12–15 years) in three time periods (7.3 years of follow-up), Netherlands Cohort Study, 1986–1993

Exposure variable	Before growth spurt				During growth spurt				After growth spurt			
	No. of cases	Person-years of observation	Rate ratio*	95% confidence interval	No. of cases	Person-years of observation	Rate ratio*	95% confidence interval	No. of cases	Person-years of observation	Rate ratio*	95% confidence interval
Hunger Winter (1944–1945)												
Residence in a nonwestern area					28	1,192	1.00†		335	3,722	1.00†	
Residence in a western rural area					14	348	1.86	0.85, 4.07	99	912	1.24	0.90, 1.71
Residence in a western city					11	521	1.01	0.46, 2.22	157	1,569	1.03	0.79, 1.35
World War II years (1940–1944)												
Residence in a rural area in 1942	6	226	1.00†		36	1,094	1.00†		227	2,219	1.00†	
Residence in a city of >40,000 in 1942	2	115	6.14	0.08, 4.80	51	1,206	1.17	0.70, 1.95	289	2,356	1.11	0.87, 1.42
Economic depression (1932–1940)												
Father had a job	340	6,255	1.00†		259	1,823	1.00†		82	436	1.00†	
Father had no job	42	714	1.10	0.74, 1.64	34	284	0.93	0.57, 1.52	11	86	0.53	0.20, 1.38

* Adjusted for age, prostate cancer in family, energy intake in 1986 (kcal/day), education, marital status, height, and β-cryptoxanthin intake in 1986 (μg/day).
† Reference category.

ods showed no pattern that differed from the overall results (data not shown). The energy restriction measures showed no consistent association with any specific subgroup of prostate cancer tumors.

DISCUSSION

In this study, we found no evidence for the hypothesis that energy restriction during adolescence is related to a decrease in prostate cancer risk. The results showed a slightly elevated prostate cancer risk among men who had lived in presumably food-restricted regions such as western cities (RR = 1.15) and western rural areas (RR = 1.30) during the Hunger Winter (1944–1945), as compared with controls living in northern and southern parts of the Netherlands who had almost no exposure to energy restriction. No association was seen with respect to the other war years (1940–1944) (RR = 1.12) or the economic depression years (RR = 0.95). In the subgroup analyses, in which subjects' exposure before, during, and after the adolescent growth spurt was evaluated, the results again showed no support for the hypothesis that energy restriction early in life plays a role in the development of prostate cancer.

Before we discuss these results in relation to those of other studies, we wish to make several relevant remarks about the Netherlands Cohort Study. Loss to follow-up is the primary source of potential selection bias in prospective cohort studies. Given the high completeness of follow-up for the cases and subcohort person-years in the Netherlands Cohort Study (20), selection bias is unlikely. Because we considered the most important potentially confounding factors reported in the literature and included in the multivariate model all factors associated with prostate cancer risk or the exposure variables (e.g., age, family history, energy intake), only unmeasured or still-unknown other factors may have caused residual confounding.

A factor that could have influenced the results is misclassification of exposure to energy restriction. Three proxy measures of energy restriction were used in this study: the employment status of the men's fathers during the economic depression years (1932–1940), residence during World War II (1940–1944), and residence during the Hunger Winter (1944–1945). Whereas surveys have shown that energy intake was associated with father's employment status in 1932–1940 (15, 16), that the food supply in the cities deteriorated much faster than that in rural areas during 1940–1944 (12, 13), and that starvation in the western part of the country in 1944–1945 was mostly confined to cities (9–11, 13), we are aware that these ecologic measures are only a proxy measure of individual exposures. However, other studies used the same proxy measure as we did for energy restriction during the Hunger Winter, and their results also indicated that our proxy measure for energy restriction in the Hunger Winter is reasonably adequate (27, 28). The finding of no association in our study could be due to a lack of variability in exposure.

In our study, the period of severe energy restriction during the Hunger Winter was relatively short (7 months of severe deprivation at less than 40 percent of normal energy intake)

(9). The short duration of energy restriction could be an explanation for our not finding an effect on prostate cancer risk. With respect to the war years (1940–1944), no association was found between living in a city and prostate cancer risk. During World War II, the food situation leveled off for everyone—people living in the city as well as people living in rural areas (29). Therefore, the contrast in energy intakes between the exposure categories could not have been sufficient to detect an effect of energy restriction in 1940–1944. Furthermore, the cohort could have been too old at the time of exposure, since during exposure in the Hunger Winter no men were under 12 years of age.

Only a few studies have examined the relation between adolescent diet and prostate cancer risk. Two studies were case-control studies (6, 8), and one was a cohort study of 14,000 Seventh-day Adventist men (7). The results of these studies are consistent with our findings. The case-control studies suggested that adolescent diet is not an important risk factor for prostate cancer but that perhaps other pubertal events affect prostate cancer risk (e.g., physical activity during childhood). Men who had diets high in saturated fatty acids as adolescents were not at increased risk for prostate cancer. It might be true that no association exits between energy restriction in adolescence and prostate cancer risk later in life.

In our study, data on physical activity in childhood were not available. Energy restriction during childhood and adolescence did have an impact on attained height and weight. Height was not a risk factor for prostate cancer in the Netherlands Cohort Study cohort, but for body mass index at age 20 years a significant positive trend in risk was observed (23). This positive association is somewhat unexpected. In general, obesity has been reported to be inversely associated with plasma testosterone levels (30–33), and lower testosterone levels may be related to lower prostate cancer risk (2). However, obesity also shows an inverse relation with sex hormone-binding globulin, and sex hormone-binding globulin is hypothesized to have an inverse association with prostate cancer risk (4). It is plausible that different hormones or hormone levels are involved at different stages in prostate cancer development. Low energy intake during childhood and adolescence may be reflected in a lower height:weight ratio at age 20 years. Our data show that weight at age 20 is related to the exposure variables, and height at baseline was also related to exposure during the Hunger Winter period (men living in a western city were not as tall as men living in a western rural area).

The subgroup analyses, with respect to different prostate cancer tumors or the timing of exposure, showed the same pattern as the overall results.

In conclusion, we found no support for the hypothesis that energy restriction in childhood and adolescence leads to a decrease in prostate cancer risk among adults living in the Netherlands. In future studies, the effects of energy restriction on prostate cancer risk should be explored among populations who experienced energy restriction for longer periods of time and earlier in life. It would also be important that exposure for each subject be repeatedly assessed throughout life to promote insight into the relation of childhood nutritional patterns to cancer risk.

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